

1-6b

WHAT IS CLAIMED IS:

1. A method of preventing or treating a disease associated with amyloid deposits of A β in the brain of a patient, comprising administering an effective dosage of an antibody that binds to an epitope within residues 1-10 of A β to the patient.

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2. The method of claim 1, wherein the disease is characterized by cognitive impairment.

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3. The method of claim 1, wherein the disease is Alzheimer's disease.

4. The method of claim 1, wherein the disease is Down's syndrome.

5. The method of claim 1, wherein the disease is mild cognitive impairment.

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6. The method claim 1, wherein the antibody is of human isotype IgG1.

7. The method of any of the preceding claims, wherein the patient is human.

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8. The method of claim 1, wherein the antibody specifically binds to an epitope within residues 1-6 of A β .

9. The method of claim 1, wherein the antibody specifically binds to an epitope within residues 1-5 of A β .

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10. The method of claim 1, wherein the antibody specifically binds to an epitope within residues 1-7 of A β .

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11. The method of claim 1, wherein the antibody specifically binds to an epitope within residues 3-7 of A β .

12. The method of claim 1, wherein the antibody specifically binds to an epitope within residues 1-3 of A β .

5 13. The method claim 1, wherein the antibody specifically binds to an epitope within residues 1-4 of A β .

14. The method of claim 1, wherein after administration the antibody binds to an amyloid deposit in the patient and induces a clearing response against the amyloid deposit.

10 15. The method of claim 14, wherein the clearing response is an Fc receptor mediated phagocytosis response.

15 16. The method of claim 15, further comprising monitoring the clearing response.

17. The method of claim 1, wherein the antibody specifically binds to an epitope comprising a free N-terminal residue of A β .

20 18. The method of claim 1, wherein the antibody binds to an epitope within residues of 1-10 of A β wherein residue 1 and/or residue 7 of A β is iso-aspartic acid.

19. The method of claim 1, wherein the patient is asymptomatic.

25 20. The method of claim 1, wherein the patient is under 50.

21. The method of claim 1, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.

30 22. The method of claim 1, wherein the patient has no known risk factors for Alzheimer's disease.

23. The method of claim 1, wherein the antibody is a human antibody.

24. The method of claim 1, wherein the antibody is a humanized antibody.

25. The method of claim 1, wherein the antibody is a chimeric antibody.

26. The method of claim 1, wherein the antibody is a mouse antibody.

27. The method of claim 1, wherein the antibody is a polyclonal antibody.

28. The method of claim 1, wherein the antibody is a monoclonal antibody.

29. The method of claim 1, further comprising administering an effective dosage of at least one other antibody that binds to a different epitope of A β .

30. The method of claim 1, wherein the isotype of the antibody is IgG1 or IgG4.

31. The method of claim 1, wherein the isotype of the antibody is IgG2 or IgG3.

32. The method of claim 1, wherein the antibody comprises two copies of the same pair of light and heavy chains.

33. The method of claim 1, wherein the antibody is a bispecific antibody comprising a first light and heavy chain pair that specifically binds to the epitope of A β and a second light and heavy chain pair that specifically binds to an Fc receptor on microglial cells.

34. The method of claim 1, wherein a chain of the antibody is fused to a heterologous polypeptide.

35. The method of claim 1, wherein the dosage of antibody is at least 1 mg/kg body weight of the patient.

36. The method of claim 1, wherein the dosage of antibody is at least 10 mg/kg body weight of the patient.

37. The method of claim 1, wherein the antibody is administered with a carrier as a pharmaceutical composition.

38. The method of claims 1, wherein the antibody is a human antibody to A β prepared from B cells from a human immunized with an A β peptide.

39. The method of claim 38, wherein the human immunized with A β peptide is the patient.

40. The method of claim 1, wherein the antibody specifically binds to A β peptide without binding to full-length amyloid precursor protein (APP).

41. The method of claim 1, wherein the antibody is administered intraperitoneally, orally, subcutaneously, intranasally, intramuscularly, topically or intravenously.

42. The method of claim 1, wherein the antibody is administered by administering a polynucleotide encoding at least one antibody chain to the patient, wherein the polynucleotide is expressed to produce the antibody chain in the patient.

43. The method of claim 1, wherein the polynucleotide encodes heavy and light chains of the antibody, which polynucleotide is expressed to produce the heavy and light chains in the patient.

44. The method of claim 1, further comprising monitoring the patient for level of administered antibody in the blood of the patient.

45. The method of any of the preceding claims, wherein the antibody is administered in multiple dosages over a period of at least six months.

46. The method of claim 1, wherein the antibody is administered as a sustained release composition.

5 47. A pharmaceutical composition comprising an antibody that specifically binds to within residues 1-10 of A β and a pharmaceutical carrier.

10 48. A method of screening an antibody for activity in treating a disease associated with amyloid deposits of A β in the brain of a patient, comprising contacting the antibody with a polypeptide comprising at least five contiguous amino acids of an N-terminal segment of A β beginning at a residue between 1 and 3 of A β , the polypeptide being free of a C-terminal segment of A β , and determining whether the antibody specifically binds to the polypeptide, specific binding providing an indication that the antibody has activity in treating Alzheimer's disease.

15 49. The method of claim 48, wherein the disease is Alzheimer's disease.

20 *Sub D3* 50. A method of screening an antibody for activity in clearing a biological entity physically associated with an antigen, comprising combining the antigen-associated biological entity, the antibody and phagocytic cells bearing Fc receptors in a medium; monitoring the amount of the antigen-associated biological entity remaining in the medium, a reduction in amount of the antigen-associated biological entity indicating the antibody has clearing activity against the antigen.

25 51. The method of claim 50, wherein the monitoring step monitors the amount of the antigen remaining in the medium.

30 52. The method of claim 50, wherein the combining comprises adding antigen-associated biological entity to the medium, and contacting the medium with the phagocytic cells bearing Fc receptors.

53. The method of any of claim 50, wherein the antigen-associated biological entity is provided as a tissue sample.

54. The method of claim 50, wherein the antigen is the biological entity.

55. The method of claim 50, wherein the tissue sample comprises an amyloid deposit.

56. The method of claim 55, wherein the tissue sample is from the brain of an Alzheimer's disease patient or a mammal animal having Alzheimer's pathology.

57. The method of claim 50, wherein the antigen is A β .

58. The method of claim 50, wherein the phagocytic cells are microglial cells.

59. The method of claim 50, wherein the tissue sample is selected from the group consisting of a cancerous tissue sample, a virally infected tissue sample, a tissue sample comprising inflammatory cells, a nonmalignant abnormal cell growth, and a tissue sample comprising an abnormal extracellular matrix.

60. A method of detecting an amyloid deposit in a patient, comprising administering to the patient an antibody that specifically binds to an epitope within amino acids 1-10 of A β and detecting the presence of the antibody in the brain of the patient.

61. The method of claim 60, wherein the antibody binds to an epitope within residues 4-10 of A β .

62. The method of claim 60, wherein the antibody binds to an epitope within residues 8-10 of A β .

63. The method of claim 60, wherein the antibody is labelled.

64. The method of claim 60, wherein the antibody is labelled with a paramagnetic label.

65. The method of claim 64, wherein the labelled antibody is detected by nuclear magnetic resonance.

66. The method of claim 64, wherein the antibody lacks capacity to induce a clearance response on binding to an amyloid deposit in the patient.

67. A diagnostic kit, comprising an antibody that specifically binds to an epitope with residues 1-10 of A β .

68. The kit of claim 67, further comprising labeling describing use of the antibody for in vivo diagnosis or monitoring of a disease associated with amyloid deposits of A β in the brain of a patient.

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add BS